

IN THE SPECIFICATION

10/593136

Please replace the paragraph bridging pages 1 -2, with:

Topical formulations comprising immunosuppressant drugs such as cyclosporine, tacrolimus, etc. and steroids such as testosterone, etc. which are highly absorbed, possess an acceptable aesthetic appeal, and are patient compliant in terms of ease of use and removal from the skin surface, have been difficult to develop, especially due to the large size of the drug molecule or ~~por~~ poor absorption through the skin. Tacrolimus is macrolide immunosuppressant produced by Streptomyces species. Cyclosporine is a cyclic polypeptide immunosuppressant agent consisting of 11 amino acids. It is produced as a metabolite by the fungus species Beauveria nlyea. No topical composition comprising cyclosporine is available in the market.

Please replace the paragraph bridging pages 7 -8, with:

The lipophilic surfactant of the present invention is selected from but not limited to the group comprising of fatty acids; sorbitan fatty acid esters; acetylated glycerol fatty acid esters; lower alcohol fatty acids esters; ~~trans-esterification~~ transesterification products of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, triglycerides and polyalkylene polyols; sterols and sterol derivatives; pentaerythritol fatty acid esters and polyalkylene glycol ethers; monoglycerides and acetylated, e.g. mono-and di-acetylated monoglycerides; or mixtures thereof.

Please replace the paragraph at page 8, line 21 (as numbered) with:

The oily components of the solvent system is selected from but not limited to natural oils, mono-, di-, or triglyceride esters of oils selected from a group consisting of medium chain triglycerides, oleic acid, ethyl oleate, ethyl caprylate, ethyl butyrate, isopropyl myristate, soyabean oil, canola oil or their mono-and di-glycerides, aluminium ~~monomonostearate~~ monostearate, aluminium ~~dimonostearate~~ distearate, aluminium ~~trimonostearate~~ tristearate,

microcrystalline wax, petroleum wax and mixtures, used either alone or in combination thereof. Preferably, the at least one oily component of the solvent system is a medium chain triglyceride.

Please replace the paragraph at page 9, line 27 (as numbered) with:

The stabilizing agent(s) useful in the present invention are selected from a group of natural and synthetic polymers and carbohydrates such as chitosan, alginates, carrageenan, cellulose derivatives, pectin, starch, xanthan gum, albumin, alginate, gelatin, acacia, cellulose dextran, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, colloidal silicon dioxide, hyaluronic acid, carboxyethyl cellulose, carboxymethyl cellulose, Poloxamer (polyethylene-propylene glycol co-polymer), ~~Cabopol~~ Carbopol (carbomer), Acrylic acid based polymers and derivatives thereof. Preferably the stabilizing agent of the present invention is Poloxamer.

Please replace the paragraph at page 10, line 26 (as numbered) with:

In another embodiment, the compositions of the present invention is meant for highly localized topical administration for hydrophobic and/or amphiphilic active ingredient(s), including but not limited to antibacterial, antifungal, anti-parasite, anti- mycotic, antibiotic, anti-inflammatory, analgesic (narcotic and non-narcotic), anti- septic, disinfectant, anti-psoriatic, anti-eczema, anti-ageing, anti-histaminic, anti-pruritic, keratolytic, anti-seborrheic, ~~gluco-corticoid~~ glucocorticoid, steroid, immunomodulators, muscle relaxant, anti-viral, anesthetic, anti-allergic, or their salts, esters, hydrates or derivatives, used either alone or in combination thereof.

Please replace the paragraph at page 11, line 24 (as numbered) with:

In the present invention, the gelator components (combination of surfactants) provide

gelation of the solvent system and thus form a three dimensional network. This is due to the fact that surfactant molecules have a tendency to associate in solvent environment leading to the formation of aggregates. These further associate with others through contact points, and thus three-dimensional networks are established, which immobilize the solvent system and acts as gel. The addition of aqueous components do not generally break these tubular and torroid toroid structures and furthermore, the stabilizing agent(s) emulsify the excess oil, which has not been gelated during the process of gelation. This also provides a cosmetic appearance to the composition. Further, this highly lipophilic microenvironment on interaction with skin lipids is intended to form a depot within the skin layers through which the entrapped hydrophobic drug could be released over an extended period of time in a localized area.

Please replace Example 5 at page 16, with:

Example 5

<i>S. No.</i>	<i>Ingredients</i>	<i>Quantity (mg/g)</i>
1.	Terbinafine hydrochloride	10.00
2.	Glyceryl monomonostearate <u>monostearate</u>	19.50
3.	Polysorbate 20	21.50
4.	Isopropyl myristate	318.50
5.	Poloxamer 188 aqueous (10% w/w) solution	0.250
6.	Benzyl alcohol	10.00
7.	Sodium metabisulphite	5.00
8.	Triethanolamine	100.00
9.	Purified water	q.s. to 1.00 g

Please replace the paragraph at page 16, line 3 (as numbered) with:

Predetermined weighed amounts of Glyceryl ~~monomonostearate~~ monostearate,

Polysorbate 20, Isopropyl myristate and Benzyl alcohol were taken. The contents were heated with continuous stirring in a constant temperature water bath while maintaining the temperature of the mass at 60-65°C. Terbinafine Hydrochloride was added in the melt, while stirring until homogenous mixing was achieved. An aqueous phase was prepared. A predetermined weighed amount of Poloxamer 188 and triethanolamine were mixed with purified water (10% w/w). To this was added Sodium metabisulphite in prescribed quantity and the mixture was stirred while maintaining the temperature of the mass at 60-65°C. The oily phase and aqueous phase were maintained at 60- 65°C and bulk of aqueous phase was added to oily phase maintaining the similar temperature (60-65°C) with continuous stirring to obtain the desired product.

Please replace Example 8 at page 18, with:

Example 8

<i>S. No.</i>	<i>Ingredients</i>	<i>Quantity (mg/g)</i>
1.	Terbinafine hydrochloride	10.00
2.	Nimesulide	10.00
2 3.	Glyceryl monomonostearate <u>monostearate</u>	250.00
3 4.	Polysorbate 20	50.00
4 5.	Propylene glycol	320.00
5 6.	Isopropyl myristate	350.00
6 7.	Benzyl alcohol	10.00

Please replace the paragraph at page 18, line 12 (as numbered) with:

Predetermined weighed amounts of Glyceryl ~~monomonostearate~~ monostearate, Polysorbate 20, Isopropyl myristate, Propylene glycol and Benzyl alcohol were taken. The contents were heated with continuous stirring while maintaining the temperature of the mass at 60-65°C. Terbinafine hydrochloride and Nimesulide were added in melt, while stirring

until homogenous mixing was achieved. The off-white to cream-colored formulation thus obtained was stored in tightly closed HDPE container.

Please replace Example 9, bridging pages 18 - 19, with:

Example 9

<i>S. No.</i>	<i>Ingredients</i>	<i>Quantity (mg/g)</i>
1.	Clotrimazole	10.00
2.	Polyethylene glycol dimonostearate <u>distearate</u>	250.00
3.	Polysorbate 20	25.00
4.	Mineral oil	250.00
5.	Chitosan	40.00
6.	Citric Acid	80.00
7.	Benzyl alcohol	10.00
8.	Purified Water	335.00

Please replace the paragraph at page 19, line 2 (as numbered) with:

An oily phase was prepared first. Predetermined weighed amounts of Polyethylene glycol ~~dimonostearate~~ distearate, Polysorbate 20, Medium chain triglyceride, Mineral oil and Benzyl alcohol were taken; the liquid ingredients were passed through nylon cloth and transferred it to a jacketed S. S. container. The solid ingredients were added to the contents of the S. S. container and mixed. This mixture was heated with continuous stirring by circulating hot water in the jacket while maintaining the temperature of the mass at 60-65°C. Clotrimazole was added in the above melt, while stirring until homogenous mixing was achieved. An aqueous phase was then prepared. Predetermined weighed amounts of Chitosan and Citric acid were mixed with sufficient purified water and the mixture was heated with continuous stirring while maintaining the temperature of the mass at 60-65°C. The oily phase and aqueous phase were maintained at 60-65°C and bulk of aqueous phase was added to oily

phase maintaining the similar temperature (60 — 65°C) with continuous stirring to obtain the desired product.

Please replace Example 10, bridging pages 19 - 20, with:

Example 10

<i>S. No.</i>	<i>Ingredients</i>	<i>Quantity (mg/g)</i>
1.	Miconazole	20.00
2.	Gentamycin sulphate	10.00
3.	Polyethylene glycol dimonostearate <u>distearate</u>	250.00
4.	Polysorbate 20	25.00
5.	Isopropyl myristate	250.00
6.	Chitosan	40.00
7.	Citric Acid	80.00
8.	Benzyl alcohol	10.00
9.	Purified Water	315.00

Please replace the paragraph at page 20, line 3 (as numbered) with:

An oily phase was prepared first. Predetermined weighed amounts of Polyethylene glycol ~~dimonostearate~~ distearate, Polysorbate 20, Isopropyl myristate and Benzyl alcohol were taken; the liquid were passed ingredients through nylon cloth and transferred to a jacketed S. S. container. The solid ingredients were added to the contents of the S. S. container and mixed. This mixture was heated with continuous stirring by circulating hot water in the jacket while maintaining the temperature of the mass at 60-65°C. Miconazole and Gentamycin sulphate were added in the above melt, while stirring until homogenous mixing was achieved. An aqueous phase was prepared. Predetermined weighed amounts of Chitosan and Citric acid were mixed with sufficient purified water and the mixture was heated with continuous stirring while maintaining the temperature of the mass at 60-65°C.

The oily phase and aqueous phase were maintained at 60-65°C and bulk of aqueous phase was added to oily phase maintaining the similar temperature (60 — 65°C) with continuous stirring to obtain the desired product.

Please replace the paragraph at page 22, line 11 (as numbered) with:

An oily phase was prepared first. Predetermined weighed amounts of Sorbitan monostearate, Polysorbate 20, Medium chain triglyceride, Butylated hydroxytoluene and Butylated hydroxyanisole were taken; the liquid ingredients were passed through nylon cloth and transferred to a jacketed S. S. container. The solid ingredients were added to the contents of the S. S. container and mixed. This mixture was heated with continuous stirring by circulating hot water in the jacket while maintaining the temperature of the mass at 50-55°C. Terbinafine hydrochloride was dissolved in methanol and added in the above melt, while stirring until homogenous mixing was achieved. An aqueous phase was then prepared. Predetermined weighed amounts of Poloxamer and Triethanolamine ~~was~~ were mixed with sufficient purified water and Benzyl alcohol was added and the mixture was heated with continuous stirring while maintaining the temperature of the mass at 50-55°C. The oily phase and aqueous phase were maintained at 60-65°C and bulk of aqueous phase was added to oily phase maintaining the similar temperature (60 — 65°C) with continuous stirring to obtain the desired formulation.